



Complete Summary

GUIDELINE TITLE

Diagnosis and initial treatment of ischemic stroke.

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Feb. 63 p. [113 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Oct. 65 p.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

- Ischemic stroke
- Transient ischemic attack (TIA)
- Symptoms of recent neurologic dysfunction suggestive of brain ischemia

GUIDELINE CATEGORY

Diagnosis
Evaluation

Management
Screening
Treatment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Internal Medicine
Neurology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To increase the percentage of patients presenting within 3 hours of stroke onset and who are evaluated within 10 minutes of arriving in the emergency department (ED)
- To increase the percentage of patients receiving appropriate thrombolytic and antithrombotic therapy for ischemic stroke (use of tissue plasminogen activator [tPA] and aspirin)
- To increase the percentage of non-tPA recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable
- To increase the percentage of patients who receive appropriate medical management for prevention of complications within the initial 24 to 48 hours of diagnosis
- To improve patient and family education of patients with ischemic stroke in both the emergency department and the admitting hospital unit

TARGET POPULATION

Patients age 18 years or older with symptoms of recent neurologic dysfunction suggestive of brain ischemia

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation/Screening

1. Emergency department (ED) or clinic evaluation, as appropriate

2. History and physical examination, including neurologic examination (use of National Institutes of Health Stroke Scale) and establishing time of symptom onset
3. Screening for tissue plasminogen activator (tPA) treatment indications and contraindications
4. Diagnostic testing, such as laboratory testing (e.g., complete blood count, electrolytes, blood urea nitrogen, creatinine, glucose, international normalized ratio, partial thromboplastin time, troponin, Aphasia Screening Test (AST), urine or serum pregnancy testing), electrocardiogram, computed tomography of the head without contrast, cardiac monitoring, oximetry
5. Other cardiac assessment (telemetry) as appropriate

Management/Treatment

1. Education of patient/family regarding diagnosis, ED process, tests, treatment and risks
2. Blood pressure (BP) management
3. Measures to treat hyperthermia or hypo- /hyperglycemia
4. Intravenous (IV) fluids (normal saline)
5. tPA
6. Aspirin (ASA) or other antithrombotics
7. Post ED management
 - Hospital care in intensive care unit or acute stroke unit/cardiac monitoring
 - Physical examinations, including vital signs and neurologic checks
 - BP management (monitoring and treating with easily titrated agents, such as labetalol, enalaprilat, enalapril, captopril, nitroprusside [Nipride])
 - Bleeding precautions
 - Monitoring for complications of therapy
 - Continued treatment of hyperthermia or hypo-/hyperglycemia
 - Continued IV fluids
 - Deep vein thrombosis prophylaxis with low dose subcutaneous heparin, low-molecular-weight heparin (e.g., enoxaparin, dalteparin), or heparinoids (e.g., danaparoid); intermittent pneumatic compression
 - Swallow evaluation
 - Early rehabilitation

MAJOR OUTCOMES CONSIDERED

- Early stroke recurrence
- Stroke progression
- Mortality due to stroke
- Disability due to stroke

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

No additional description of literature search strategies is available.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Study Quality Designations

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline annotation, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member groups during an eight-week review period.

Each of the Institute's participating member groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are

developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating member groups following implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

Guideline Work Group

Following the completion of the review period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary, and a written response is prepared to address each of the responses received from member groups. Two members of the Cardiovascular Steering Committee carefully review the input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of four questions: (1) Is there consensus among all ICSI member groups and hospitals on the content of the guideline document? (2) Has the drafting work group answered all criticisms reasonably from the member groups? (3) Within the knowledge of the appointed reviewer, is the evidence cited in the document current and not out-of-date? (4) Is the document sufficiently similar to the prior edition that a more thorough review (critical review) is not needed by the member group? The committee then either approves the guideline for release as submitted or negotiates changes with the work group representative present at the meeting.

Pilot Test

Member groups may introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer, and other practice systems. Evaluation and assessment occur throughout the pilot test phase, which usually lasts for three to six months. At the end of the pilot test phase, ICSI staff and the leader of the work group conduct an interview with the member groups participating in the pilot test phase to review their experience and gather comments, suggestions, and implementation tools.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline, and the Cardiovascular Steering Committee reviews the revised guideline and approves it for release.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations for the diagnosis and initial treatment of ischemic stroke are presented in the form of four algorithms with 40 components, accompanied by detailed annotations. Algorithms are provided for: [Screening \(Ambulatory\)](#), [Emergency Department](#), [Stroke Code](#), [Ischemic Stroke Emergency Department Management \(not a thrombolysis candidate\)](#); clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) and conclusion grade (I-III, Not Assignable) definitions are repeated at the end of the "Major Recommendations" field.

Clinical Highlights and Recommendations

1. Patients who present in time to be candidates for treatment with tissue plasminogen activator (tPA) should be evaluated by a physician within 10 minutes, undergo a computed tomography (CT) scan within 25 minutes of arrival in the emergency department (ED), and have CT interpreted within 20 minutes of test completion. (Annotations #20, 25)
2. Intravenous (IV) tPA, if given, should be administered within 3 hours of stroke onset and less than 60 minutes of arrival at the ED. (Annotations #20, 21, 23, 25, 26)
3. Patients presenting with stroke onset who are not candidates for IV tPA should promptly be given aspirin, after exclusion of hemorrhage on CT scan. (Annotation # 31)
4. Education regarding early stroke symptoms, risk factors, diagnostic procedures, and treatment options should be offered to the patient and family. This should be documented in the patient chart. (Annotation #27)
5. Medical management for prevention of complications; within the initial 24 to 48 hours of diagnosis and initial treatment of ischemic stroke include:
 - continue appropriate blood pressure management
 - continue to treat hyperthermia;
 - continue to treat hypo or hyperglycemia;
 - continue IV fluids;
 - initiate deep vein thrombosis prophylaxis;
 - perform swallow evaluation;
 - initiate early rehabilitation.

Screening (Ambulatory) Algorithm Annotations

2. Immediate Screening for Ischemic Stroke

This should include detail as to the location, severity, duration of symptoms, and any aggravating or relieving factors. Symptoms that are commonly associated with ischemic stroke or transient ischemic attack (TIA) diagnoses include: *

- Sudden numbness or weakness of the face, arm, or leg--especially on one side of the body
- Sudden mental confusion, trouble speaking or understanding
- Sudden trouble walking, dizziness, loss of balance or coordination
- Sudden trouble seeing in one or both eyes
- Sudden severe headache with no known cause

* List from American Stroke Association for public education

Less common symptoms that may represent ischemic stroke or TIA include sudden onset vertigo, double vision, nausea or vomiting, stupor or coma, difficulty swallowing, a hoarse voice, and/or shaking of a limb.

3. Symptoms Consistent with New Ischemic Stroke, TIA or Unsure?

Clinical diagnoses with neurologic symptoms that may imitate or superficially resemble ischemic stroke or TIA include:

- Migraine
Neurologic symptoms experienced with migraine tend to have a more gradual onset and slower development. However, the two problems may be indistinguishable.
- Seizures
Although seizures typically consist of a "positive" phenomenon (jerking of a limb) rather than loss of neurologic function (weakness or paralysis of a limb), symptoms and signs during the ictus or in the postictal state may be similar to ischemic stroke (e.g., confusion or speech arrest during the ictus as in complex partial seizure, postictal confusion, postictal paralysis, and other sensory or visual phenomenon.)
- Syncope
- Transient global amnesia
This is characterized by a sudden onset antegrade and retrograde memory disturbance without other focal neurologic symptoms. If the patient experiences symptoms of transient global amnesia it would be inappropriate to assume the diagnosis without a complete neurologic exam.
- Peripheral nerve disorders
Mononeuropathy and radiculopathy can be distinguished from ischemic stroke by the anatomic distribution of the symptoms and in the case of radiculopathy by the associated painful symptoms. Bell's palsy, vestibular neuritis and extraocular muscle imbalance due to cranial neuropathy may also imitate ischemic stroke and require a complete history and neurologic examination to accurately differentiate from ischemic stroke.
- Intracranial hemorrhage
- Other intracranial masses (e.g., tumor, abscess [often differentiated by CT])
The mode of onset and early course tend to be more gradual in development.
- Neuroses
Neuroses such as anxiety or panic disorder may need to be considered in some cases.
- Metabolic disorders
Hypoglycemia is the most common metabolic disorder producing neurologic symptoms that imitate stroke. A patient with known diabetes or liver disease should be screened for hypoglycemia.

This discussion is not meant to represent a detailed guide to discerning between ischemic stroke and other diagnoses. If there is any uncertainty as to symptom causation, the evaluation should proceed as though ischemic stroke or TIA is confirmed so as not to delay appropriate emergency treatment if needed.

6. Possible Cerebral Infarct, Symptoms Onset Within 24 Hours?

Key Point:

- The onset of symptoms should be defined as the last time the patient was known to be normal or at previous pre-stroke baseline.

If the symptoms resolve completely and then recur, for the purposes of determining whether thrombolysis can be considered for stroke, the time of onset would be the last time the patient was normal (just prior to the onset of the second set of symptoms). Patients may be unable to give this information if they have an aphasia or mental confusion. Family members or other witnesses may need to give this information. If the patient was sleeping and awoke with the problem, the time of onset would be the moment the patient was last known to be normal just before falling asleep.

7. Possible Cerebral Infarct, Symptoms Mild and Stable > 24 Hours?

Patients with stable mild deficits present longer than 24 hours may be transported to the ED for evaluation and treatment by means other than 911. As a rule, they should be admitted to the hospital to assure thorough and expeditious evaluation and treatment. Outpatient evaluation and treatment is an acceptable alternative if it can be done as quickly as it could be done inpatient and if all goals of inpatient assessment (diagnosis of mechanism, initiation of appropriate secondary prevention, prevention of complications, early assessment for and deployment of rehabilitative services) can be successfully addressed.

10. Possible TIA, Symptoms Occurred Within Last 2 Hours?

Patients presenting with history suggestive of TIAs may have neurological deficits they are unaware of. To avoid missing the thrombolytic treatment window, patients with possible TIAs presenting within 2 hours of symptom onset should be triaged like patients with stroke.

11. Possible TIA, Symptoms Occurred >2 Hours, but Within Last 48 Hours?

This work group recommends that the physician strongly consider hospitalization for TIA patients who appear in the ED within 48 hours of the event to expedite work-up and possibly administer tPA if the deficit recurs.

12. Transport to Emergency Department by 911 or Other Means

Patients should be taken to the ED urgently.

13. Possible TIA, or Symptoms Occurred >48 Hours, but Within Last 2 Weeks?

Patients with a single episode of transient ischemic symptoms greater than 48 hours from presentation but within the last two weeks should be considered for an expedited outpatient evaluation within 72 hours. Those with several TIAs (greater than 4) in that time frame require immediate evaluation and hospitalization.

Recommendation:

- If less than two hours past event, dial 911

- If two hours to 48 hours past event, may be transported to ED by family or friend

14. Other Factors Suggesting High Risk for Immediate Future Events?

Key Points:

- Risk of stroke is greatest in the immediate aftermath of TIA or minor stroke
- Features of presentation define those at highest risk
- Hospitalization should be strongly considered for those at highest risk

Recent reports highlight the frequent early recurrence of symptoms of stroke and other cardiovascular events as well as the value of early intervention. Whether hospitalization would help to mitigate further injury by ensuring appropriate surgical intervention when needed (carotid endarterectomy) or increasing the percentage of patients receiving appropriate prophylaxis early in their course is not clear. However, it would seem prudent to admit most patients to the hospital with transient ischemic attack that occurred within 48 hours of presentation in order to expedite their evaluation and address these issues promptly given the immediate risk of recurrence described above. Furthermore, hospitalization would enable timely administration of lytic therapy in the interval of greatest risk, the initial 24 to 48 hours. The factors outlined above which predict high risk of recurrence might influence decision making in this patient group. Although the data available cannot define an appropriate triage decision for all patients, this information should serve as a guide for appropriate and safe management of the patient with TIA. Certain diagnostic entities if suspected may require hospitalization for specific management even with presentation later than 24 hours from TIA occurrence (e.g., carotid or vertebral artery dissection, specific coagulopathy or arteriopathy, cerebral venous thrombosis.)

In summary, the Committee recommends consideration of hospitalization for patients with first TIA within the past 24 to 48 hours to facilitate early deployment of lytic therapy, if necessary, and to expedite institution of definitive secondary prevention. For others, multiple and increasingly frequent symptoms ("crescendo TIAs") and the clinical features described above might also justify hospitalization rather than expedited ambulatory management. Whatever the strategy, speed is key. Patients managed in the outpatient setting should be fully educated about the need to return immediately if symptoms recur to allow use of lytic therapy.

Evidence supporting this recommendation is of classes: B, D, M, R

15. Should be Seen in Clinic Within 72 Hours

Patients with fewer than five TIAs within a two-week time frame may be evaluated by a physician within 72 hours. A more emergent evaluation with hospitalization is indicated if there are features suggestive of crescendo TIAs or factors predictive of a high risk of future events. (See Annotation #14, "Other Factors Suggesting High Risk for Immediate Future Events?")

Refer to the Support for Implementation section, "Recommended Website Resources" in the original guideline document.

16. For Symptoms Occurring > 2 Weeks Ago, Clinic Appointment Within One Week

Risk of recurrence in this group may be lower than those with early presentation. Prompt outpatient evaluation by a physician within one week is appropriate.

Refer to the Support for Implementation section, "Recommended Website Resources" in the original guideline document.

Refer to Annotation #14, "Other Factors Suggesting High Risk for Immediate Future Events?"

Emergency Department Treatment Algorithm Annotations

20. Symptom Onset Allows for Evaluation and Treatment Within 180 Minutes (with Thrombolysis IV)?

Key Points:

- Patients presenting to the ED within 150 minutes of symptom onset should be evaluated rapidly for treatment with IV tPA
- Occasionally, patients may be able to receive tPA even if they present later than 150 minutes if their work-up such as laboratory evaluation has been completed and they have other aspects such IV access in place
- In any case, treatment should begin within 3 hours (180 minutes) of symptom onset

Patients presenting to the ED soon after the onset of symptoms may be candidates for treatment with IV tissue plasminogen activator (tPA) and will therefore require a rapid evaluation and treatment initiation. Although the time window from onset of symptoms to treatment can be up to 180 minutes, the evaluation in the ED will require at least 30 minutes in most cases (CT scan of head, laboratory tests performed and results returned, IV access obtained, and neurological exam and history). The guideline committee has therefore chosen 150 minutes as a practical cutoff time for this triage decision. Those who are not candidates for thrombolytic therapy could be evaluated according to usual ED routine.

There are important exceptions to this time limitations guideline for triage of the patients into the "Stroke Code" process. In certain instances, the time for evaluation may be shorter and this time limit of 150 minutes for triage to "Stroke Code" evaluation may be too conservative and should be 165 or 170 minutes. One example would be the patient who is already in the hospital and has received the appropriate laboratory evaluation, who already has an IV access, and for whom much of the history is already known. In that case, a brief neurologic exam and rapid evaluation with CT may be the only items

required prior to treatment and could theoretically be performed in 10 to 15 minutes.

Refer to the original guideline document for information on tPA tested in large, randomized, placebo-controlled clinical trials.

Evidence supporting this recommendation is of classes: A, C, D, R

21. Intra-Arterial Thrombolytic Candidate? (Option Available?)

Key Points:

- Intra-arterial thrombolysis is an option for patients with middle cerebral artery (MCA) or basilar artery (BA) occlusions presenting beyond the 3-hour time window for intravenous tPA (i.e., 3 to 6 hours for MCA, 3 to 12 hours for BA).
- There is no proof of superiority of the intra-arterial therapy over intravenous therapy within 3 hours.
- A combined intravenous/intra-arterial approach for the 3-hour window is under study.

Intra-arterial thrombolytic therapy may be a treatment option for selected patients presenting in an early time frame but beyond the 3-hour time window for intravenous tPA. This is not a routine treatment. The availability of this option will be institution dependent, and patients must be highly selected. If considering this treatment option for a patient, physicians must explain to patients and family that this is an experimental treatment with substantial risk. Despite the limitations of available study data, in cases of more severe presentation with middle cerebral artery (MCA) or basilar artery occlusion, intra-arterial thrombolytic treatment may be appropriate since the prognosis without treatment is poor.

If the patient is an appropriate candidate for this treatment, consideration should be given to immediate transfer to an institution offering this intervention. If an endovascular interventionist skilled in this technique is available to the hospital, this person should be mobilized quickly.

See the original guideline document for criteria for consideration of angiographic evaluation for intra-arterial treatment.

Please note that the management during and following intra-arterial treatment is outside the scope of this guideline.

Evidence supporting this recommendation is of classes: A, C, D

23. See [Stroke Code Algorithm](#)

The goal of the stroke code is to rapidly administer tPA in appropriately screened candidates. The onset of symptoms to treatment can be up to 180 minutes, but the National Institutes of Health (NIH) recommendation of "door to drug" is within 60 minutes.

Stroke Code Algorithm Annotations

25. Stroke Code

Key Points:

- "Door to first physician contact" for thrombolytic candidates is within 10 minutes.
- "Door to initiation of CT scan" for thrombolytic candidates is within 25 minutes.
- "Door to drug" for thrombolysis treatment is within 60 minutes.

The guideline committee uses the term "stroke code" to refer to a process in the ED for the rapid evaluation and treatment of patients who have presented in a time frame qualifying them for thrombolytic therapy. This process may take many forms. It might include a formal "stroke team" that is called whenever a possible candidate for tPA has presented or it may include the ED staff who have been trained in the rapid evaluation and treatment of stroke victims. The general concept is one which includes:

- Rapid triage of patients as soon as they arrive in the ED
- Immediate initiation of phlebotomy for appropriate blood tests followed by CT scan
- First physician contact for history and exam occurring early in the ED visit. The NIH recommendation for timing of "door to first physician contact" for thrombolytic candidates is within 10 minutes.
- Rapid access to the best neurologic and radiologic expertise available at the individual institution for evaluation of the patient and the CT scan prior to treatment. This may include a neurologist and neuroradiologist present at the time of treatment. Alternatively, it may be a primary care physician with expertise in stroke diagnosis and administration of tPA and a general radiologist with expertise in reviewing head CT scans for early infarct change. The NIH recommendation for the timing of "door to initiation of CT scan" for thrombolytic candidates is within 25 minutes.
- The goal of the stroke code should be to rapidly administer tPA in appropriately screened candidates. The NIH recommendation for the timing of "door to drug" for thrombolytic treatment is within 60 minutes.

26. Evaluation (Should Occur Concurrently with Intervention)

Key Points:

- Review tPA indications/contraindications and document whether patient is eligible.
- Perform National Institutes of Health Stroke Scale (NIHSS).
- Draw blood for lab tests.
- Perform EKG.
- Perform noncontrast head CT to exclude hemorrhage.

- Review History and Tissue Plasminogen Activator Treatment Indications and Contraindications

Take a complete patient history including a review of indications and contraindications for treatment with tPA. The contraindications for treatment should be considered relative contraindications.

The recommendations for treatment indications and contraindications were modified from the Institute for Clinical Systems Improvement (ICSI) Technology Assessment Work Group for tPA for Acute Ischemic Stroke. They are based upon the National Institute of Neurologic Disorders and Stroke (NINDS) study recommendations with amendments to include recommendations from clinical practice at Mayo Clinic and treatment guidelines from the Stroke Treatment in the Community study.

See "[ICSI Tissue-type plasminogen activator for acute ischemic stroke](#)" TA # 28, 1996.

Evidence supporting this recommendation is of class: D

- Indications for tPA
 - Acute onset of focal neurologic symptoms in a defined vascular territory, consistent with ischemic stroke
 - Clearly defined onset of stroke less than 3 hours prior to planned start of treatment; if the patient awakens with symptoms, onset is defined as the time of the last known baseline neurological status
 - Eighteen years of age or older
 - CT scan does not show evidence of intracranial hemorrhage, nonvascular lesions (e.g., brain tumor, abscess) or signs of advanced cerebral infarction such as sulcal edema, hemispheric swelling, or large areas of low attenuation consistent with acute stroke
- Contraindications for tPA

Clinical Contraindications

- Clearly defined onset of stroke greater than 3 hours prior to planned start of treatment; if the patient awakens with symptoms, onset is defined as the time of the last known baseline neurological status
- Rapidly improving symptoms
- Mild stroke symptoms/signs (National Institute of Health Stroke Scale [NIHSS] less than 4)

Examples include:

- Sensory symptoms only
- Ataxia without other deficits
- Dysarthria without other deficit

- Mild motor signs (non-disabling)
- Visual field defect without other deficit
- In the setting of middle cerebral artery (MCA) stroke, an obtunded or comatose state may be a relative contraindication.
- Seizure at onset of stroke symptoms or within the 3 hours prior to tPA administration
- Clinical presentation suggestive of subarachnoid hemorrhage regardless of CT result
- Hypertension--systolic blood pressure (SBP) greater than 185 mm Hg or diastolic blood pressure (DBP) greater than 110 mm Hg

Patients with this blood pressure (BP) excluded only if it remains elevated on consecutive measurements. Also exclude if aggressive treatment is required to lower BP into appropriate range

History Contraindications

- Minor ischemic stroke within the last month
- Major ischemic stroke or head trauma within the last 3 months
- History of intracerebral or subarachnoid hemorrhage if recurrence risk is substantial
- Untreated cerebral aneurysm, arteriovenous malformation (AVM), or brain tumor
- Gastrointestinal or genitourinary hemorrhage within the last 21 days
- Arterial puncture at a noncompressible site within the last 7 days or lumbar puncture within the last 3 days
- Major surgery or major trauma within the last 14 days
- Clinical presentation suggestive of acute myocardial infarction (MI) or post-MI pericarditis
- Patient taking oral anticoagulants and international normalized ratio (INR) greater than 1.7
- Patient receiving heparin within the last 48 hours and having an elevated activated partial thromboplastin time (aPTT)
- Patient receiving low-molecular-weight heparin within the last 24 hours
- Pregnant, or anticipated pregnant, female
- Known hereditary or acquired hemorrhagic diathesis or unsupported coagulation factor deficiency
- Received tPA less than 7 days previously

Laboratory Contraindications

Glucose should always be measured prior to giving tPA; other parameters should be checked before treatment if there is reason to believe they may be abnormal (e.g., INR and aPTT should be checked if patient has been exposed recently to warfarin or heparin or if there is history of liver disease).

- Glucose less than 50 or greater than 400 mg per deciliter

- Platelet count less than 100,000 per cubic millimeter
- INR greater than 1.7
- Elevated aPTT
- Positive pregnancy test

Radiology Contraindications

- Intracranial hemorrhage
- Large area of low attenuation and/or effacement of cerebral sulci consistent with new or evolving stroke may be a relative contraindication.
- Intracranial tumor, aneurysm, arteriovenous malformation (AVM) or other space-occupying lesion

Once indications and contraindications have been reviewed, documentation of why patient was included or excluded must occur.

- Perform Neurologic Examination and Vital Signs Every 15 Minutes

A history and neurological examination must be performed to assess whether the presentation is consistent with a stroke diagnosis and to estimate the severity of the deficit. Use of the National Institutes of Health Stroke Scale (NIHSS) by physicians and nursing staff is encouraged as this would provide a uniform method of evaluation for comparison between examiners during the early hours of the stroke evaluation. The guideline committee encourages use of the NIHSS as an initial evaluation tool and after resuscitation or treatment to assess for change.

The NIHSS is a quantitative measure of neurologic deficit in stroke patients that covers the key aspects of the neurological exam including level of consciousness and orientation, eye movements, visual fields, facial weakness, motor strength in limbs, coordination, sensation, language and comprehension of language, articulation, and neglect. It can be performed in rapid fashion (5-8 minutes) which is an important feature in this clinical setting.

Evidence supporting this recommendation is of classes: B, C, D, R

Refer to the original guideline document for additional details.

- Record Estimated Weight
- Draw Blood for Lab Tests

Recommended laboratory tests include:

- complete blood count (CBC) and platelet count
- electrolytes, blood urea nitrogen (BUN), creatinine
- Point of Care (P.O.C.) glucose

- INR and partial thromboplastin time (PTT)

Others to consider:

- Troponin
- Aphasia Screening Test (AST)

These tests are used to evaluate for dehydration, metabolic disorders which might influence neurologic status (especially hypoglycemia and hyperglycemia), hematologic disorders such as polycythemia which may affect cerebral perfusion, or coagulopathies which could affect the treatment decision. Prior to administration of tPA the platelet count and glucose level should be reviewed. If the patient is known to be on warfarin or has received heparin within the last 24 hours, the prothrombin time and partial thromboplastin time should be reviewed prior to treatment. A urine or serum pregnancy test should be obtained in women of child bearing potential if there is substantial reason to believe the patient may be pregnant.

- Perform Electrocardiogram

An electrocardiogram should be performed for the purpose of screening for concomitant cardiac disease, either acute or chronic which may impact on immediate treatment decisions.

- Perform CT Head Without Contrast

A CT scan without contrast must be performed prior to treatment with tPA, primarily for the purpose of excluding hemorrhage. Early signs of infarct should also be sought, as this finding confers greater risk of symptomatic intracerebral hemorrhage with tPA treatment. It is suggested that the greatest level of radiologic expertise possible be obtained for this reading with the caveat that this CT reading should not create excessive delays in the evaluation and treatment process. A process for rapid teleradiography CT readings should be organized and in place if needed.

- Other Cardiac Assessment as Appropriate (Telemetry)

27. Intervention (Should Occur Concurrently with Evaluation)

Key Points:

- Educate and document education of patient and caregiver.
- BP management for non-tPA candidates.
- BP management for tPA candidates.
- Maintain euvolemia with isotonic fluids.
- Correct hyperthermia, hypo- or hyperglycemia, and hypoxia.
- Educate Patient and Family

A process should be in place for the patient and family that will rapidly orient them to the suspected diagnosis, ED process, tests to be performed, tPA treatment and its risks, and other treatment measures to be considered. This could include both caregiver face-to-face interaction with the patient and family as well as teaching tools in written form. Education should be documented in the medical record.

- Treat Hypertension if greater than 185 systolic and 110 diastolic

Patients with this BP excluded only if it remains elevated on consecutive measurements. Also exclude if aggressive treatment is required to lower BP into appropriate range (e.g., if more than a few doses of any medication is required or if nitroprusside drip is required.)

Recommendations for Management of BP in the setting of acute ischemic stroke, tPA candidate:

- No tPA if DBP greater than 140 on 2 readings, 5 min apart and use nitroprusside to control blood pressure
- Treat SBP greater than 185 or DBP greater than 110 using easily titrated agents (labetalol, enalapril). Do not use tPA if BP is difficult to lower below these thresholds

Refer to the original guideline document for discussion of supporting evidence and the American Heart Association (AHA) recommendations for the management of patients with acute ischemic stroke.

In general, discontinuation of a patient's usual daily antihypertensive regimen is not advised as this may result in unwanted rebound hypertensive effects. Exceptions to this practice might include holding these medications if the BP is low and holding diuretic therapy regardless of the BP, to avoid any problems with volume depletion that might contribute to hemoconcentration that could limit blood flow.

Evidence supporting this recommendation is of classes: A, D, R

- Initiate 2 IV lines

Two intravenous (IV) lines should be started so that tPA may have a dedicated line

- Start IV Fluids

Treatment with a 0.9% normal saline at a rate of 75 to 125 cc/hr or 2-3 L/day should be administered for the avoidance of dehydration. The rate may be adjusted for febrile patients.

Evidence supporting this recommendation is of classes: A, C, D, R

- Treat Hyperthermia

Interventions for patients with temperatures of greater than 37.5 degrees C (99.5 degrees F) include appropriate dosing of acetaminophen (1 gram orally or 650 mg rectally every 4-6 hours, not to exceed 4-6 grams in 24 hours) and regular monitoring of temperature status (every 4 hours). For those patients with extreme hyperthermia greater than 39.4 degrees C (103 degrees F), aggressive interventions including cooling blankets and ice packs are encouraged. Secondary causes for temperature elevation should be sought.

In human studies, early hyperthermia in acute stroke is associated with increased risk of poor outcome, higher mortality, and increased infarct volume. The causality and the relationship of temperature elevation to these poor outcomes are not fully understood. Whether intervention with cooling methods will result in improved outcomes is unknown. [Conclusion Grade III: See Conclusion Grading Worksheet - Appendix A - Annotation #27 (Hyperthermia) in the original guideline document]

Evidence supporting this recommendation is of classes: B, D, M, R

- Treat Hyperglycemia

Hyperglycemia may adversely influence clinical outcome.

- Early identification of patients with hyperglycemia in the setting of acute ischemic stroke or in those at risk for cerebral ischemia (ED evaluation of glucose level) is recommended.
- Avoid any agents or factors which might induce hyperglycemia.
 - Eliminate glucose from any IV solutions used. (Recommend use of normal saline.)
 - Avoid use of corticosteroids, even in those patients with cerebral edema, as it is unlikely to be helpful and may be harmful. Separate recommendations are needed for those on maintenance corticosteroid dosing for concurrent conditions and treatment decisions are left to the clinical discretion of the physician.
- Use appropriate measures to maintain euglycemia, carefully avoiding hypoglycemia.
- Continue to monitor glucose with bedside testing in those receiving treatment in order to maintain euglycemia.

It is unclear whether early hyperglycemia in the setting of acute stroke may be a marker of physiologic stress or an independent predictor of poor outcome. Usual management of hyperglycemia with gentle dosing of subcutaneous insulin in a timely manner during acute ischemia would seem prudent until ongoing clinical trials address the appropriateness of more aggressive treatment measures. [Conclusion Grade III: See Conclusion Grading Worksheet - Appendix B - Annotation #27D (Hyperglycemia) in the original guideline document]

Evidence supporting this recommendation is of classes: A, B

28. Patient Meets Criteria for tPA, Has No Contraindications and Symptom Onset Still Less Than 3 Hours?

Refer to Algorithm Annotation #26, "Evaluation (Should Occur Concurrently With Intervention)," for criteria.

29. Initiate Tissue Plasminogen Activator (tPA)

Treatment should consist of tPA 0.9 mg/kg intravenously to a maximum dose of 90 mg. Ten percent of this dose should be given as a bolus over 1 to 2 minutes and the remainder infused over one hour. This dosing may be based upon actual or estimated weight.

31. Initiate Aspirin or Other Antithrombotics

Key Points:

- Aspirin (ASA) should be given rectally or via nasogastric (NG) tube promptly in patients who are not rt-PA candidates unless contraindicated (ASA allergy, gastrointestinal (GI) bleeding).
- There is no evidence to support therapeutic anticoagulation with unfractionated heparin, low-molecular weight (LMW) heparin or heparinoids. There is as yet insufficient evidence to decide whether specific subgroups of ischemic stroke (e.g., dissection, cardio-embolism with intra-cardiac clot) will benefit from therapeutic anticoagulation.
- If a decision is made to use continuous heparin infusion, boluses should be avoided and aPTT should be maintained in the 1.5-2 times baseline range.
- No anti-coagulation or anti-platelet should be given when CT/MRI shows a hemorrhagic stroke. This recommendation applies to ischemic stroke due to arterial occlusion; hemorrhagic transformation in the setting of sinovenous infarction is not necessarily a contraindication to antithrombotic therapy including heparin.
- Low dose prophylactic anticoagulation (e.g., unfractionated heparin 5000 units subcutaneously (SQ) twice daily) is beneficial for prevention of deep vein thrombosis (DVT) or pulmonary embolism (PE) in stroke patients with limited mobility.

Aspirin (ASA)

Patients who are not candidates for tPA should be promptly given ASA in a dose of 325 mg orally, rectally, or by nasogastric tube and should be continued on a similar daily dose. Exceptions to this approach would include avoiding treatment in those with contraindications to ASA therapy (e.g., ASA allergy, gastrointestinal hemorrhage).

Evidence supporting this recommendation is of classes: A, M

Considerations with Heparin Use

Results from the International Stroke Trial provide powerful evidence against the routine use in patients with acute ischemic stroke, of any heparin regimen as intensive as the moderate dose subcutaneous regimen utilized in this very large clinical trial (unfractionated heparin - 12,500 units subcutaneous twice daily).

This would include the adjusted dose continuous infusion of unfractionated heparin that is commonly employed for the treatment of stroke in the United States. The commonly cited indication of vertebrobasilar distribution ischemia or ischemic stroke in the setting of atrial fibrillation was analyzed separately and there was no measurable benefit in these specific subgroups. Similarly, the weight of available data regarding use of full dose low-molecular-weight heparin for the acute treatment of stroke do not support their routine use for limiting disability or decreasing mortality in this setting.

The routine use of acute anticoagulation treatment with unfractionated heparin, low-molecular-weight heparin, or heparinoid in acute ischemic stroke is not supported by the available evidence. This treatment does not appear to improve clinical outcome from the index stroke. There may be subgroups who benefit, but further studies of this problem are required for confirmation. [Conclusion Grade I: See Conclusion Grading Worksheet - Appendix C - Annotation #31 (Heparin) in the original guideline document]

Despite these discouraging results, the use of continuous heparin infusion in acute stroke has continued to be common in clinical practice. Given these data, if the decision is made to use full dose continuous heparin infusion for a specific indication (e.g., large vessel atherothrombosis or dissection), physicians are strongly recommended to discuss with their patients the lack of proof for this therapy and to detail the potential hazards of therapy. Lower doses of these agents, e.g., enoxaparin 40 mg subcutaneously daily or unfractionated heparin 5,000 IU subcutaneously BID, are beneficial for the prevention of deep vein thrombosis or pulmonary embolus in those stroke victims with limited mobility and can be advocated for that purpose.

Evidence supporting this recommendation is of classes: A, R

32. Post-Emergency Department Medical Management (Post-Thrombolysis)

- Admit to intensive care unit or acute stroke care unit/cardiac monitoring.
- Perform vital signs and neurologic checks every 15 minutes for 2 hours, then every 30 minutes for 6 hours, then every 60 minutes for 24 hours (recommend use of an abbreviated National Institutes of Health Stroke Scale [NIHSS] for neurologic checks).
- Treat BP if greater than 180/105
 - First 24 hours: Treat if SBP greater than 180 or DBP greater than 105.
 - Greater than 24 hours: Treat if SBP greater than 220, mean arterial pressure (MAP) greater than 130.
 - Monitor BP and any corresponding neurologic changes in the ED and first few days of hospitalization
- Initiate bleeding precautions:

- Avoid placement of central venous access or arterial puncture for the first 24 hours.
- Placement of an indwelling bladder catheter should be avoided during drug infusion and for at least 30 minutes after infusion ends.
- Insertion of a nasogastric tube should be avoided, if possible, during the first 24 hours.
- Avoid use of anticoagulant, antiplatelet, or non-steroidal anti-inflammatory agents for the first 24 hours.
- Monitor for central nervous system (CNS) hemorrhage
- If any signs of CNS hemorrhage (e.g., neurologic deterioration, development of severe headache, sudden severe elevation of BP, or new nausea or vomiting) or signs of major systemic hemorrhage institute the following measures:
 - Discontinue infusion of thrombolytic drug.
 - Obtain hemoglobin, hematocrit, partial thromboplastin time, prothrombin time/INR, platelet count, fibrinogen (also type and cross match if transfusions will be needed).
 - Obtain surgical consultation if necessary.
 - Obtain emergent CT head without contrast if central nervous system hemorrhage suspected.
- Initiate other anti-thrombotic therapy 24 hours after tPA administration (antiplatelet agent or anticoagulant as appropriate).

33. Post-Emergency Department Medical Management (Not a Thrombolysis Candidate)

Treat BP if greater than 220/120 or MAP greater than 130

Recommendations - Ischemic stroke, not a tPA candidate:

- Treat BP only if SBP greater than 220, MAP greater than 130.
- Use easily titrated agents, choosing those with the least effect on cerebrovasculature (labetalol, enalaprilat). American Heart Association (AHA) recommendations support oral dosing, but if swallowing is affected IV agents should be used.

Note: Dosing examples are included in the original guideline document.

- Avoid agents which tend to cause precipitous drops in BP (e.g., sublingual calcium channel blockers).
- Treat hypotension (IV fluids, treat congestive heart failure or arrhythmia and consider pressors).
- Monitor BP and any corresponding neurologic changes in the ED and first few days of hospitalization. Avoid overtreating BP.

It is important to recognize that these recommendations must be tailored to the individual, dependent on the patient's acute presentation and whether or not there is a previous history of hypertension. Young patients without a previous history of hypertension may be less tolerant of the higher extremes of BP in this setting. Specific comorbidities which may require a more aggressive use of antihypertensive therapy in this setting include:

- Left ventricular failure
- Aortic dissection
- Acute myocardial ischemia
- Renal insufficiency induced by accelerated hypertension
- Hypertensive encephalopathy
- Hemorrhagic conversion of an ischemic infarct
- Thrombolytic treatment

In general, discontinuation of a patient's usual daily antihypertensive regimen is not advised as this may result in unwanted rebound hypertensive effects. Exceptions to this practice might include holding these medications if the BP is low and holding diuretic therapy regardless of the BP, to avoid any problems with volume depletion that might contribute to hemoconcentration that could limit blood flow.

34. Other Post-Emergency Department Medical Management (First 24-48 Hours)

- Continue to treat hyperthermia, hyperglycemia, or hypoglycemia

Refer to Annotation #27, "Intervention", above.

- Initiate deep vein thrombosis (DVT) prophylaxis

Consider DVT prophylaxis in any patient admitted to the hospital with weakness related to an ischemic stroke. The risk of DVT is high (25-50%), and prophylaxis with subcutaneous heparin decreases the incidence (10 to 20%). The risk of pulmonary embolism appears to be decreased as well, although numbers have been small and statistical significance not achieved

Unfractionated subcutaneous heparin at 5,000 units every 12 hours is the standard dose; 5,000 Units every 8 hours has been used in larger individuals. Low- molecular-weight heparin and heparinoids may be slightly more effective for DVT prophylaxis (decreased incidence from 22% with heparin to 13% with enoxaparin or danaparoid), and theoretically potentially safer (less risk of bleeding), but it has not been conclusively demonstrated in studies. Low-molecular-weight heparin is renally cleared; dose should be modified with renal insufficiency. Intermittent pneumatic compression devices should be considered in individuals who are not candidates for anticoagulation (patients with a bleeding diathesis or at risk of gastrointestinal bleeding).

Evidence supporting this recommendation is of class: M

- Perform swallow evaluation

Early evaluation of swallow should be performed in patients at risk of aspiration so that an appropriate diet adjustment may be instituted. Patients at risk include those with facial weakness, significant

dysarthria, excessive drooling, sputtering, choking, gurgling, wet voice, or pocketing food in mouth. Clear liquids by mouth and in some cases any food or fluid should be avoided in this setting until a swallow evaluation has established the patient's level of risk for aspiration with the various consistencies.

Swallow evaluation and dietary adjustments based on this information and early mobilization as effective treatments for prevention of medical complications have not been adequately evaluated in randomized clinical trials. However, in the absence of this level of proof, since these interventions are safe and have a reasonable probability of improving care by decreasing complications, it is reasonable to advocate their use in this setting. Several previously published guidelines advocate these practices

- Initiate rehabilitation early

Early mobilization within 48 hours of admission is advocated by means of early initiation of appropriate rehabilitation swivels or other nursing intervention for the purpose of preventing complications related to immobility including deep vein thrombosis, contractures, joint disorders, and pressure sores/decubitus ulcers.

Evidence supporting this recommendation is of class: R

[Ischemic Stroke Emergency Department Management \(not a thrombolysis candidate\) Algorithm Annotations](#)

38. Patient Requires Hospital Admission?

Key Points:

- Hospitalization should be considered even in patients with subacute minor stroke to arrange secondary prevention and address potential complications

Patients with acute ischemic stroke or TIA (occurring less than 24 to 48 hours before presentation) should generally be admitted to the hospital unless it is clearly based on expert opinion that outpatient evaluation and treatment is appropriate.

In patients with ischemic stroke occurring days to weeks prior to initial clinical evaluation with stable neurologic deficits, admission to the hospital is not always required. However, the following comorbidities or complications should be considered as possible reasons for admission to the hospital.

- Significant impairment of activities of daily living that render return to home unsafe
- Suspected medical complications of stroke such as aspiration pneumonia, deep vein thrombosis, cardiac dysrhythmia, urinary tract

infection, dehydration, rhabdomyolysis or other problems requiring medical intervention

- Other medical comorbidities such as uncontrolled diabetes, uncontrolled hypertension or unstable ischemic cardiac disease or dysrhythmia
- Cause for stroke unclear and hospital admission necessary to expedite evaluation for causation
- Inadequate anticoagulation in patients with atrial fibrillation

Please refer to Annotation #14, "Other Factors Suggesting High Risk for Immediate Future Events?"

Definitions:

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Nonrandomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided for:

- [Screening \(Ambulatory\)](#)
- [Emergency Department Treatment](#)
- [Stroke Code](#)
- [Ischemic Stroke Emergency Department Management \(not a thrombolysis candidate\)](#)

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The guideline contains an annotated bibliography and discussion of the evidence supporting each recommendation. The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations (i.e., choice among alternative therapeutic approaches) is graded for each study.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate screening and referral for patients presenting with neurological symptoms
- Rapid evaluation and treatment of patients who are candidates for thrombolytic therapy
- Improved management of ischemic stroke
- Effective prevention of stroke progression/recurrence
- Decreased mortality and morbidity associated with ischemic stroke

POTENTIAL HARMS

Adverse effects of thrombolytic drugs can include signs of central nervous system hemorrhage (e.g., neurologic deterioration, development of severe headache, sudden severe elevation of blood pressure, or new nausea or vomiting) or signs of major systemic hemorrhage.

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications for Tissue Plasminogen Activator (tPA)

Clinical Contraindications

- Clearly defined onset of stroke greater than 3 hours prior to planned start of treatment; if the patient awakens with symptoms, onset is defined as the time of the last known baseline neurological status
- Rapidly improving symptoms
- Mild stroke symptoms/signs. Examples include: sensory symptoms only, ataxia without other deficits, dysarthria without other deficit, mild motor signs (non-disabling), and visual field defect without other deficit
- In the setting of middle cerebral artery stroke, an obtunded or comatose state may be a relative contraindication.
- Seizure at onset of stroke symptoms or within the 3 hours prior to tPA administration
- Clinical presentation suggestive of subarachnoid hemorrhage regardless of computed tomography result
- Hypertension--systolic blood pressure (SBP) greater than 185 mm Hg or diastolic blood pressure (DBP) greater than 110 mm Hg. Patients with this blood pressure (BP) excluded only if it remains elevated on consecutive

measurements. Also exclude if aggressive treatment is required to lower blood pressure into appropriate range.

History Contraindications

- Minor ischemic stroke within the last month
- Major ischemic stroke or head trauma within the last 3 months
- History of intracerebral or subarachnoid hemorrhage if recurrence risk is substantial
- Untreated cerebral aneurysm, arteriovenous malformation (AVM), or brain tumor
- Gastrointestinal or genitourinary hemorrhage within the last 21 days
- Arterial puncture at a noncompressible site within the last 7 days or lumbar puncture within the last 3 days
- Major surgery or major trauma within the last 14 days
- Clinical presentation suggestive of acute myocardial infarction (MI) or post-myocardial infarction pericarditis
- Patient taking oral anticoagulants and international normalized ratio (INR) greater than 1.7
- Patient receiving heparin within the last 48 hours and having an elevated activated partial thromboplastin time
- Patient receiving low-molecular-weight heparin within the last 24 hours
- Pregnant, or anticipated pregnant, female
- Known hereditary or acquired hemorrhagic diathesis or unsupported coagulation factor deficiency
- Received tPA less than 7 days previously

Laboratory Contraindications

- Glucose less than 50 or greater than 400 mg per deciliter
- Platelet count less than 100,000 per cubic millimeter
- INR greater than 1.7
- Elevated activated partial thromboplastin time (aPTT)
- Positive pregnancy test

Radiology Contraindications

- Intracranial hemorrhage
- Large area of low attenuation and/or effacement of cerebral sulci consistent with new or evolving stroke may be a relative contraindication.
- Intracranial tumor, aneurysm, arteriovenous malformation (AVM) or other space-occupying lesion

Contraindications to Aspirin (ASA) Therapy

- Aspirin allergy
- Gastrointestinal hemorrhage

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.
- Hyperthermia. In human studies, early hyperthermia in acute stroke is associated with increased risk of poor outcome, high mortality, and increased infarct volume. The causality and the relationship of temperature elevation to these poor outcomes is not fully understood. Whether intervention with cooling methods will result in improved outcomes is unknown.
- Hyperglycemia. It is unclear whether early hyperglycemia in the setting of acute stroke may be a marker of physiologic stress or an independent predictor of poor outcome. Usual management of hyperglycemia with gentle dosing of subcutaneous insulin in a timely manner during acute ischemia would seem prudent until ongoing clinical trials address the appropriateness of more aggressive treatment measures.
- Heparin. The routine use of acute anticoagulation treatment with unfractionated heparin or low-molecular-weight heparin in acute ischemic stroke is not supported by the available evidence. This treatment does not appear to improve clinical outcome from the index stroke. There may be subgroups who benefit, but further studies of this problem are required for confirmation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for release, a member group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

The following aims were identified by the guideline work group as key areas in which medical groups may receive benefits in implementing this guideline.

Priority Aims and Suggested Measures

1. Increase the percentage of patients presenting within 3 hours of stroke onset who are evaluated within 10 minutes of arriving in the emergency department (ED).

Possible measure for accomplishing this aim:

- a. Percentage of patients presenting within 3 hours of stroke onset who are evaluated with 10 minutes of arriving in the ED.
2. Increase the percentage of patients receiving appropriate thrombolytic and antithrombotic therapy for ischemic stroke (use of tissue plasminogen activator [tPA] and aspirin).

Possible measures for accomplishing this aim:

- a. Percentage of eligible patients presenting with ischemic stroke treated with tPA.
 - b. Percentage of patients who are not candidates for tPA treatment who receive aspirin within 24 hours of hospitalization, after a negative head computed tomography (CT) scan, unless contraindicated.
 - c. Percentage of patients receiving tPA who are treated according to guideline (refer to Annotations #29 and 32)
 - d. Percentage of patients who are candidates for tPA with a "door to drug" time (time of arrival to time of drug administration) of less than 60 minutes.
 - e. Percentage of patients who undergo CT scan within 25 minutes of arrival in the ED.
3. Increase the percentage of non-tPA recipients who have hypertension appropriately managed in the first 48 hours of hospitalization or until neurologically stable.

Possible measure for accomplishing this aim:

- a. Percentage of non-tPA recipients who have hypertension appropriately managed according to the guideline (refer to Annotation #33).
4. Increase the percentage of patients who receive appropriate medical management for prevention of complications within the initial 24-48 hours of diagnosis including:
 - continue to treat hypoglycemia or hyperglycemia
 - continue to treat hyperthermia
 - continue intravenous fluids
 - continue to treat hypoxia
 - initiate deep vein thrombosis prophylaxis
 - perform swallow evaluation
 - initiate early rehabilitation (early mobilization)

Possible measures for accomplishing this aim:

- a. Percentage of patients who receive appropriate intervention for hypoglycemia and hyperglycemia.
 - b. Percentage of patients who receive appropriate intervention for hyperthermia
 - c. Percentage of patients who receive intravenous fluids.
 - d. Percentage of patients who receive appropriate treatment for hypoxia
 - e. Percentage of patients with paralysis or other reason for immobility receiving appropriate prevention for venous thromboembolism (subcutaneous heparin or pneumatic compression device).
 - f. Percentage of patients who are at risk for aspiration who receive an early swallow evaluation.
 - g. Percentage of patients mobilized from bed within 48 hours of admission.
5. Improve patient and family education of patients with ischemic stroke in both the ED and the admitting hospital unit.

Possible measures for accomplishing this aim:

- a. Percentage of patients presenting in the ED with ischemic stroke onset for whom patient/family education is documented in the medical record.
- b. Percentage of patients admitted to a hospital unit with ischemic stroke for whom patient/family education has been documented in the medical record.

At this point in development for this guideline, there are no specifications written for possible measures listed above. The Institute for Clinical Systems Improvement will seek input from the medical groups on what measures are of most use as they implement the guideline. In a future revision of the guideline, one or two measurement specifications may be included.

Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Hospitals should consider developing and implementing critical pathways, standing orders and a stroke process to accomplish rapid evaluation and treatment.
 - a. Established process for expediting the evaluation and treatment of patients who are candidates for intravenous (IV) tPA
 - b. Presence of standing orders for acute stroke to include:
 - Ongoing antithrombotic therapy
 - Management of blood pressure
 - Early mobilization
 - Use of appropriate anti-embolism treatment in the paralyzed patient
2. A process should be in place for the patient and family that will rapidly orient them to the suspected diagnosis, ED process, tests to be performed, tPA

treatment and its risks, and other treatment measures to be considered. This could include both caregiver face-to-face interactions with the patient and family as well as teaching tools in written form.

IMPLEMENTATION TOOLS

Clinical Algorithm
Pocket Guide/Reference Cards

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Feb. 63 p. [113 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Oct (revised 2005 Feb)

GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health

System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

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GUIDELINE COMMITTEE

Cardiovascular Steering Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, ICSI has adopted a policy of revealing relationships work group members have with companies that sell products or

services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline. Readers of the guideline may assume that only work group members listed below have potential conflict of interest to disclose.

No work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at www.icsi.org.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version: Diagnosis and initial treatment of ischemic stroke. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2003 Oct. 65 p.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](http://www.icsi.org).

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ICSI pocket guidelines. April 2004 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2004. 404 p.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

PATIENT RESOURCES

None available

NGC STATUS

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